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Article

Cyclopalladated ferrocenylimines with ester groups for Heck and Suzuki coupling reactions

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ABSTRACT

Cyclopalladated ferrocenylimine dimers and cyclopalladated ferrocenylimine monomers were designed and prepared. They were characterized using ¹H NMR, ¹³C NMR, and IR spectroscopies, and MS. The catalytic properties of these compounds in Heck and Suzuki coupling reactions in water or organic solvents were systematically investigated. The results showed that these catalysts could effectively catalyze Heck and Suzuki coupling reactions of aryl or heteroaryl halides in water or organic solvents.

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1. Introduction

The palladium-catalyzed Suzuki and Heck coupling reactions of aryl halides are important and versatile methods for the generation of C–C bonds [1–7] and have been used extensively in the synthesis of natural products, pharmaceuticals, herbicides, and advanced materials [8,9]. The Suzuki coupling reaction is useful because of its tractability, high stability, mild reaction conditions, and broad functional group tolerance, as well as the low toxicity of boron compounds [10–14]. Generally, palladium-catalyzed Heck and Suzuki reactions are performed in polar organic solvents under oxygen-free conditions because of the solubility of the substrate and instability of most catalysts. However, from economic and environmental standpoints, it is desirable to use water as a solvent instead of hazardous and expensive organic solvents [15]. It is therefore worthwhile developing new highly active catalysts that are not

sensitive to air and moisture, as well as easy to recover and recycle [16–19]. Some significant advances have been made in meeting these requirements, including the use of phase-transfer catalysts [20–22], water-soluble phosphine ligands [23,24], water as a cosolvent [25,26], and amphiphilic polymers for catalyst immobilization [27]. More recently, microwave heating [28] and ultrasonic irradiation [29] have been used as tools in synthetic chemistry to facilitate C–C coupling in water. However, many of these procedures use expensive and complex ligands, supports, or external assistance such as microwave heating or ultrasonic irradiation, and, with a few exceptions, most reactions involve hazardous organic cosolvents. To the best of our knowledge, only a few studies have shown that Suzuki and Heck coupling reactions could be carried out efficiently using ligand-free palladium catalysts under conventional heating in neat water. For instance, the protocol for a Suzuki coupling reaction using 2.5 mol% of Na₂PdCl₄, with the addition of so-

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dium dodecyl sulfate as a surfactant, in pure water under aerobic conditions at 100 °C was reported by Ranu et al. [20]. Marziale et al. [30] developed an efficient method for Suzuki coupling reactions catalyzed by a palladacyclic catalyst precursor produced by *ortho* palladation of ([1,1'-biphenyl]-2-yloxy) diisopropylphosphine, enabling the reaction to be performed in neat water under air and at ambient temperature with Pd loadings of 0.04 mol%. Basu et al. [21] found that a combination of Pd(OAc)₂ and tetra-*n*-butylammonium bromide in water at ambient temperature showed high catalytic activity in the reactions of aryl bromides or iodides with aryl trihydroxyborate salts of sodium at catalyst loading of 0.5 mol%. The key to the coupling reaction was the use of aryl trihydroxyborate salts of sodium to increase the substrate solubility in pure water. The protocol for Suzuki and Heck reactions catalyzed by 0.1 mol% palladium supported on a magnetic microgel in water at 90 °C was reported by Yu et al. [31]; however, the attractiveness of their method is limited because it requires an argon atmosphere. In addition, Roglans et al. [32] demonstrated that PdCl₂(CH₃CN)₂ was an efficient catalyst for Suzuki and Heck coupling reactions in water at room temperature or 40 °C; however, arenediazonium salts were used as substrates, and the amount of palladium catalyst used was high, 5–10 mol%. From the academic and industrial viewpoints, the design of catalytic systems using simple ligand-free palladium catalysts without other external assistance in neat water is therefore still a promising route for establishing greener C–C coupling reactions [22].

In our previous studies, we synthesized a series of cyclopalladated ferrocenylimines, which showed satisfactory reactivities in Heck, Suzuki, Sonogashira, and Kumada reactions [33–41]. However, there has recently been considerable interest in the development of new and simple catalysts that can effectively catalyze C–C coupling reactions in water or aqueous media because such catalysts have the potential to be used in industrial systems. In this paper, the preparation and catalytic properties of cyclopalladated ferrocenylimines with ester groups are reported. The results show that these compounds effectively catalyze Heck and Suzuki coupling reactions with catalyst loadings of 0.1 mol% under ligand-free and ambient

conditions in water or organic solvents.

2. Experimental

2.1. General

All chemicals were purchased from commercial companies. *N,N*-Dimethylformamide (DMF), toluene, and methanol were dried with MgSO₄, filtered, distilled, and stored over 4 Å molecular sieves. Melting points were measured using a WC-1 microscopic apparatus and were uncorrected. IR spectra were recorded with a Bruker VECTOR22 spectrometer using KBr pellets. Mass spectra were recorded using an LC-MSD-Trap-XCT instrument. ¹H and ¹³C NMR spectra were recorded in CDCl₃ using a Bruker DPX-400 spectrometer with tetramethylsilane (TMS) as the internal standard. The GC yields were determined using *n*-dodecane internal standards. GC analyses were carried out using a Shimadzu GC-2010 Plus instrument. All the Suzuki and Heck coupling reactions were performed without the protection of an inert gas.

2.2. Preparation of compounds

Cyclopalladated ferrocenylimines were prepared as shown in Scheme 1.

2.2.1. Preparation of ferrocenylimines

A mixture of acetylferrocene (5.0 mmol), *p*-aminoethylbenzoate (5.0 mmol) or *m*-aminoethylbenzoate (5.0 mmol), molecular sieve (4 Å, 4.0 g), and toluene (80 mL) was refluxed for 24 h at 120 °C under a nitrogen atmosphere. The volume of the solution was reduced to ca. 10 mL. The products were separated and purified on a chromatography column with petroleum ether and ethyl acetate (2:1) as the eluent.

[(η⁵-C₅H₅)Fe(η⁵-C₅H₄CMe=NC₆H₄-*p*-COOEt)]. Yield, 80%; deep-red solid; m.p. 122–124 °C; IR (KBr pellet): 2922, 2846, 1704, 1627, 1594, 1100, 816, 714 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.04–8.02 (2H, m, C₆H₄), 6.80 (2H, d, *J* = 8.4 Hz, C₆H₄), 4.79 (2H, t, *J* = 1.8 Hz, C₅H₄), 4.46 (2H, t, *J* = 1.8 Hz, C₅H₄), 4.40–4.35 (2H, m, CH₂CH₃), 4.23 (5H, s, C₅H₅), 2.08 (3H, s,

Scheme 1. Syntheses of cyclopalladated ferrocenylimines.

CH₃–C=N–), 1.40 (3H, t, *J* = 5.2 Hz, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 168.1, 166.6, 156.3, 130.7, 125.1, 119.4, 83.0, 71.0, 69.9, 69.6, 68.4, 60.7, 58.5, 30.1, 18.3, 14.4; MS: Calcd for C₂₁H₂₁FeNO₂ [*M* + 1]⁺ 376.1, found 376.7.

[(η⁵-C₅H₅)Fe(η⁵-C₅H₄CMe=NC₆H₄-*m*-COOEt)]. Yield, 85%; red oil; IR (KBr pellet): 2922, 2846, 1704, 1627, 1594, 1461, 1365, 880, 780, 700 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.74 (1H, d, *J* = 7.1 Hz, C₆H₄), 7.40 (1H, s, C₆H₄), 7.30 (1H, t, *J* = 7.4 Hz, C₆H₄), 6.90 (1H, d, *J* = 7.7 Hz, C₆H₄), 4.79 (2H, s, C₅H₄), 4.45 (2H, m, C₅H₄), 4.30–4.25 (2H, m, CH₂CH₃), 4.20 (5H, s, C₅H₅), 2.22 (3H, s, CH₃–C=N–), 1.29 (3H, t, *J* = 7.1 Hz, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 166.0, 164.6, 160.4, 148.3, 131.0, 129.5, 120.6, 114.3, 80.8, 70.2, 68.3, 62.0, 60.9, 20.5, 14.1; MS: Calcd for C₂₁H₂₁FeNO₂ [*M* + 1]⁺ 376.1, found 376.7.

2.2.2. Preparation of cyclopalladated ferrocenylimines

Cyclopalladated dimers (**1a** and **2a**) were prepared as follows. A mixture of Li₂PdCl₄ (1.0 mmol), sodium acetate (1.0 mmol), and ferrocenylimine (1.1 mmol) in methanol (10 mL) was stirred for 24 h at room temperature. The mixture was filtered and the obtained solid was washed with ethanol. The products were separated and purified by chromatography column, using dichloromethane and ethanol (2:1) as the eluent.

[PdCl₂[(η⁵-C₅H₅)Fe[(η⁵-C₅H₃)CMe=NC₆H₄-*p*-COOEt]]]₂ **1a**. Yield, 90%; deep-red solid; m.p. > 218 °C (dec); IR (KBr pellet): 2925, 1274, 1168, 1104, 1017, 816 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.09 (2H, d, *J* = 7.4 Hz, C₆H₄), 7.14 (2H, d, *J* = 7.2 Hz, C₆H₄), 4.66 (1H, s, C₅H₃), 4.41 (5H, s, C₅H₅), 4.38 (1H, s, C₅H₃), 4.33 (1H, s, C₅H₃), 4.27–4.21 (2H, m, CH₂CH₃), 1.99 (3H, s, CH₃–C=N–), 1.43 (3H, t, *J* = 6.8 Hz, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 179.8, 166.5, 165.1, 153.4, 131.4, 128.9, 122.4, 101.2, 91.5, 73.8, 71.3, 66.4, 65.9, 61.1, 53.2, 52.4, 21.6, 14.9; MS: Calcd for C₄₂H₄₀Cl₂Fe₂N₂O₄Pd₂ [*M*–Cl]⁺ 994.9, found 995.1.

[PdCl₂[(η⁵-C₅H₅)Fe[(η⁵-C₅H₃)CMe=NC₆H₄-*m*-COOEt]]]₂ **2a**. Yield, 80%; deep-red solid; m.p. > 260 °C (dec); IR (KBr pellet): 2925, 1274, 1168, 1104, 1017, 880, 780, 700 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.76 (1H, d, *J* = 7.8 Hz, C₆H₄), 7.45 (1H, s, C₆H₄), 7.39 (1H, t, *J* = 7.8 Hz, C₆H₄), 6.95 (1H, d, *J* = 7.8 Hz, C₆H₄), 4.81–4.78 (2H, m, C₅H₅), 4.46–4.41 (2H, m, C₅H₃), 4.37 (2H, q, *J* = 7.1 Hz, CH₂CH₃), 4.23 (5H, s, C₅H₃), 2.08 (3H, s, CH₃–C=N–), 1.38 (3H, t, *J* = 7.1 Hz, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 179.8, 166.5, 165.1, 153.4, 131.4, 128.9, 122.4, 101.2, 91.5, 73.8, 71.3, 66.4, 61.1, 53.2, 52.4, 21.6, 14.9; MS: Calcd for C₄₂H₄₀Cl₂Fe₂N₂O₄Pd₂ [*M*–Cl]⁺ 994.9, found 995.1.

Cyclopalladated ferrocenylimine monomers (**1b** and **2b**) were prepared as follows. A mixture of **1a** or **2a** (0.5 mmol) and triphenylphosphine (1.5 mmol) in dichloromethane (10 mL) was stirred for 1 h. The volume of the solution was reduced to ca. 3 mL. The products were purified on a chromatography column with dichloromethane as the eluent.

[PdCl₂[(η⁵-C₅H₅)Fe[(η⁵-C₅H₃)CMe=NC₆H₄-*p*-COOEt]](PPh₃)] **1b**. Yield, 91%; deep-red solid; m.p. > 180 °C (dec); IR (KBr pellet): 2925, 1274, 1168, 1104, 1017, 810, 760, 684 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.06 (2H, d, *J* = 8.4 Hz, C₆H₄), 7.81–7.71 (6H, m, PPh₃), 7.43–7.35 (9H, m, PPh₃), 7.08 (2H, d, *J* = 8.1 Hz, C₆H₄), 4.48 (1H, d, *J* = 2.2 Hz, C₅H₃), 4.35 (2H, m, CH₂CH₃), 4.16 (1H, t, *J* = 2.2 Hz, C₅H₃), 3.94 (5H, s, C₅H₅), 3.43

(1H, d, *J* = 2.2 Hz, C₅H₃), 2.08 (3H, s, CH₃–C=N–), 1.36 (3H, t, *J* = 7.1 Hz, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 179.8, 166.5, 165.1, 153.4, 135.0, 132.4, 131.4, 130.3, 128.9, 127.9, 122.4, 101.2, 91.5, 73.8, 71.3, 66.4, 61.1, 53.2, 52.4, 21.6, 14.9; MS: Calcd for C₃₉H₃₅ClFeNO₂PPd [*M*–Cl]⁺ 742.1, found 742.1.

[PdCl₂[(η⁵-C₅H₅)Fe[(η⁵-C₅H₃)CMe=NC₆H₄-*m*-COOEt]](PPh₃)] **2b**. Yield, 79%; deep-red solid; m.p. 138–140 °C; IR (KBr pellet): 2925, 1274, 1168, 1104, 1017, 880, 780, 700 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.87 (1H, d, *J* = 7.8 Hz, C₆H₄), 7.80–7.71 (6H, m, PPh₃), 7.65 (1H, s, C₆H₄), 7.48–7.37 (9H, m, PPh₃), 7.37–7.34 (1H, m, C₆H₄), 7.26 (1H, s, C₆H₄), 5.29 (1H, s, C₅H₃), 4.48 (1H, d, *J* = 2.3 Hz, C₅H₃), 4.35 (2H, q, *J* = 7.1 Hz, CH₂CH₃), 4.16 (1H, t, *J* = 2.0 Hz, C₅H₃), 3.94 (5H, s, C₅H₅), 2.09 (3H, s, CH₃–C=N–), 1.38 (3H, t, *J* = 7.1 Hz, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 179.8, 166.0, 148.3, 132.4, 131.0, 130.3, 128.0, 127.9, 120.6, 119.9, 114.3, 101.2, 91.5, 73.8, 71.3, 66.4, 60.9, 53.2, 52.4, 14.1; MS: Calcd for C₃₉H₃₅ClFeNO₂PPd [*M*–Cl]⁺ 742.1, found 742.1.

2.3. General procedure for Suzuki coupling reactions of aryl bromides with phenylboronic acid

A mixture of aryl bromide (0.5 mmol), phenylboronic acid (0.6 mmol), base (1 mmol), catalyst **1a** (0.1 mol%), and solvent (2 mL) was stirred at a specified temperature under air. The reaction mixture was stirred for 2 h and then diluted with water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted three times with ethyl acetate. The combined organic phase was dried with MgSO₄ and filtered; the solvent was removed using a rotary evaporator. The crude product was transferred to a 10 mL volumetric flask to fix its quantity in ethyl acetate. Yields of the desired cross-coupling products were determined by GC using *n*-dodecane (10 mL, 0.5 mmol) as an internal standard. The products were isolated using thin-layer chromatography. The ¹H NMR spectroscopy and melting point data of the products were identical to those of commercially available authentic samples.

2.4. General procedure for Heck reactions of aryl halides with styrene

An aryl halide (0.5 mmol) and styrene (2 mmol) were combined with a base (0.5 mmol), *n*-Bu₄NBr (0.5 mmol), and catalyst **1a** (0.1 mol%) in a small round-bottomed flask. The reaction mixture was stirred at a specified temperature under air for 6 h and then diluted with water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted three times with ethyl acetate. The combined organic phase was dried with MgSO₄ and filtered, and the solvent was removed using a rotary evaporator. The crude product was transferred to a 10 mL volumetric flask to fix its quantity in ethyl acetate. Yields of the desired cross-coupling products were determined by GC using *n*-dodecane (10 mL, 0.5 mmol) as an internal standard. The products were isolated using thin-layer chromatography. The ¹H NMR spectroscopy and melting point data of the products were identical to those of commercially available authentic samples.

3. Results and discussion

3.1. Heck coupling reactions in organic solvents

The coupling of 4-bromobenzene with styrene catalyzed by **1a** was selected as a model reaction. As shown in Table 1, NaOAc as the base and DMF as the solvent afforded the highest yield (Table 1, entry 8). The relative activities of palladacycles **1a**, **1b**, **2a**, and **2b** in the coupling reaction of 4-bromobenzene with styrene in the presence of NaOAc as the base in DMF were examined. The results showed that the catalytic activities of these cyclopalladated complexes were similar, but catalyst **1a** was slightly more active under the same reaction conditions (entries 8–11).

The couplings of a number of other aryl bromides were conducted in the presence of 0.1 mol% **1a**, using the optimized conditions described above; the results are shown in Table 2. The reactions of aryl bromides containing electron-withdrawing groups such as –CN, –CHO, –NO₂, and –CF₃ gave the coupling products in modest to high yields (entries 1 and 8–17). Aryl bromides with electron-rich groups such as –OMe, –NH₂, and –CH₃ were poor coupling partners or almost inactive under the same reaction conditions (entries 2–7). When heterocyclic compounds such as 1-bromonaphthalene, 3-bromothiophene,

Table 1

Investigation of Heck cross-coupling reaction conditions.

Entry	Base	Solvent	T (°C)	Yield ^a (%)	TON	TOF (h ⁻¹)
1	Na ₂ CO ₃	DMF	130	91		
2	K ₃ PO ₄	DMF	130	66		
3	KOH	DMF	130	61		
4	K ₃ PO ₄ ·3H ₂ O	DMF	130	48		
5	Et ₃ N	DMF	130	35		
6	K ₂ CO ₃	DMF	130	30		
7	NaHCO ₃	DMF	130	87		
8	NaOAc	DMF	130	> 99	990	165
9 ^b	NaOAc	DMF	130	95	950	158
10 ^c	NaOAc	DMF	130	98	980	163
11 ^d	NaOAc	DMF	130	94	940	157
12	NaOAc	dioxane	110	74		
13	NaOAc	CH ₃ OH:H ₂ O = 1:1	90	94		
14	NaOAc	DMSO	140	16		
15	NaOAc	toluene	110	6		
16	NaOAc	methanol	70	72		
17	NaOAc	THF	70	65		

Reaction conditions: PhBr (0.5 mmol), styrene (2.0 mmol), catalyst **1a** (0.1 mol%), base (0.5 mmol), *n*-Bu₄NBr (0.5 mmol), solvent (2.0 mL), under air for 6 h.

^a GC yields. ^b Catalyst **1b** (0.1 mol%). ^c Catalyst **2a** (0.1 mol%). ^d Catalyst **2b** (0.1 mol%).

Table 2

Heck cross-coupling reactions of aryl bromides with styrene.

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Reaction conditions: aryl bromides (0.5 mmol), styrene (2.0 mmol), catalyst **1a** (0.1 mol%), NaOAc (0.5 mmol), *n*-Bu₄NBr (0.5 mmol), DMF (2.0 mL), at 130 °C under air for 6 h.

^a GC yields. ^b Isolated yields.

and 3-bromopyridine were used as substrates, the cross-coupling products were obtained in modest to excellent yields (entries 18–20). The results showed that complex **1a** was an efficient catalyst for Heck cross-coupling reactions of aryl bromides in organic solvents.

3.2. Heck coupling reactions in water

The coupling reaction of 4-bromobenzene with styrene, catalyzed by palladacycle **1a**, was selected as a model reaction. As shown in Table 3, when NaOAc was used as the base in water, the yield was excellent (entry 8). The relative activities of several palladacycles for the same model reaction, using NaOAc and water, were then studied, and we found that **1a** exhibited the highest activity (entries 8–11).

We further investigated the Heck coupling reactions between a range of aryl bromides and styrene in water; the results are shown in Table 4. The reactions of electron-deficient aryl bromides with *para* substituents such as $-\text{CN}$, $-\text{CHO}$, $-\text{NO}_2$, and $-\text{CF}_3$ gave the coupling products in modest to high yields

Table 3

Investigation of Heck cross-coupling reaction conditions in water.

Entry	Base	Solvent	<i>T</i> (°C)	Yield ^a (%)	TON	TOF (h ⁻¹)
1	Na ₂ CO ₃	H ₂ O	100	71		
2	K ₃ PO ₄	H ₂ O	100	92		
3	KOH	H ₂ O	100	88		
4	K ₃ PO ₄ ·3H ₂ O	H ₂ O	100	94		
5	(CH ₃) ₃ ONa	H ₂ O	100	88		
6	K ₂ CO ₃	H ₂ O	100	66		
7	NaHCO ₃	H ₂ O	100	67		
8	NaOAc	H ₂ O	100	>99	990	165
9 ^b	NaOAc	H ₂ O	100	91	910	152
10 ^c	NaOAc	H ₂ O	100	98	980	163
11 ^d	NaOAc	H ₂ O	100	93	930	155
12	NaOAc	H ₂ O	100	83		
13	NaOAc	H ₂ O	90	90		

Reaction conditions: PhBr (0.5 mmol), styrene (2 mmol), catalyst **1a** (0.1 mol%), base (0.5 mmol), *n*-Bu₄NBr (0.5 mmol), H₂O (2.0 mL), under air for 6 h. ^a GC yields. ^b Catalyst **1b** (0.1 mol%). ^c Catalyst **2a** (0.1 mol%). ^d Catalyst **2b** (0.1 mol%).

Table 4

Heck cross-coupling reactions of aryl bromides with styrene in water.

Entry ^a	ArX	Product	Yield ^a (%)	Yield ^b (%)	Entry ^a	ArX	Product	Yield ^a (%)	Yield ^b (%)
1	C ₆ H ₅ Br		>99	98	14	<i>p</i> -CF ₃ -C ₆ H ₄ Br		91	86
2	<i>o</i> -CH ₃ -C ₆ H ₄ Br		5.0		15	<i>p</i> -NO ₂ -C ₆ H ₄ Br		96	92
3	<i>p</i> -CH ₃ -C ₆ H ₄ Br		10		16	3-Br-pyridine		98	92
4	<i>m</i> -NH ₂ -C ₆ H ₄ Br		32		17	3-Br-furan		76	
5	<i>p</i> -NH ₂ -C ₆ H ₄ Br		83	80	18	3-Br-thiophene		76	
6	<i>o</i> -OCH ₃ -C ₆ H ₄ Br		5.0		19	Bromo-naphthalene		16	
7	<i>p</i> -OCH ₃ -C ₆ H ₄ Br		7.0		20	<i>p</i> -CH ₃ CO-C ₆ H ₄ Cl		58	
8	<i>o</i> -CHO-C ₆ H ₄ Br		34		21	<i>o</i> -NO ₂ -C ₆ H ₄ Cl		28	
9	<i>m</i> -CHO-C ₆ H ₄ Br		58		22	1-chloro-2,4-dinitrobenzene		42	
10	<i>p</i> -CHO-C ₆ H ₄ Br		96	92	23	<i>o</i> -CH ₃ O-C ₆ H ₄ Cl		7	
11	<i>o</i> -CN-C ₆ H ₄ Br		51		24	<i>m</i> -CH ₃ -C ₆ H ₄ Cl		23	
12	<i>m</i> -CN-C ₆ H ₄ Br		33		25	<i>p</i> -CH ₃ O-C ₆ H ₄ Cl		80	
13	<i>p</i> -CN-C ₆ H ₄ Br		>99	94					

Reaction conditions: aryl bromides (0.5 mmol), styrene (2.0 mmol), catalyst **1a** (0.1 mol%), NaOAc (0.5 mmol), *n*-Bu₄NBr (0.5 mmol), DMF (2.0 mL), at 130 °C under air for 6 h. ^a GC yields. ^b Isolated yields.

(entries 1, 10, and 13–15), and those with *ortho* or *meta* substituents gave lower yields (entries 8, 9, 11, and 12). Aryl bromides with electron-rich groups such as –OMe, –NH₂, and –CH₃ exhibited lower reactivities under the same reaction condition (entries 2–4, 6, and 7), but 4-bromoaniline gave the coupling product in 83% yield (entry 5). When heteroaryl bromides such as 3-bromofuran and 3-bromopyridine were used as substrates, the coupling products were obtained in modest to excellent yields, but 1-bromonaphthalene was found to be a poor coupling partner under the same reaction conditions, giving only 16% yield (entries 16–19). Finally, the reactions of aryl chlorides with styrene in water were also investigated. Aryl chlorides gave the corresponding coupling products in low yields (entries 20–24). However, 1-chloro-4-methoxybenzene reacted with styrene to give the coupling product in 80% yield (entry 25).

3.3. Suzuki cross-coupling reactions in organic solvents

Suzuki cross-coupling reactions of 4-bromotoluene and phenylboronic acid were carried out using various bases and solvents in the presence of 0.1 mol% of **1a** without the protection of an inert gas; the results are shown in Table 5. As can be seen from Table 5, the reaction proceeded smoothly in toluene, and among the tested bases, KOH was found to be the most effective (entry 2). The relative activities of several palladacycles under the same reaction conditions were investigated, using KOH as the base and toluene as the solvent (entries 2–5). The palladacycles all exhibited high catalytic activities for Suzuki coupling reactions under the optimized reaction conditions.

Catalyst **1a** was used to catalyze the Suzuki coupling reactions between aryl bromides and phenylboronic acid in toluene; the results are shown in Table 6. Electron-deficient or

Table 5

Investigation of Suzuki cross-coupling reaction conditions.

$\text{H}_3\text{C}-\text{C}_6\text{H}_4-\text{Br} + \text{C}_6\text{H}_5-\text{B}(\text{OH})_2 \xrightarrow[\text{Solvent, } T]{\text{Cat. } \mathbf{1a}, \text{ base}} \text{H}_3\text{C}-\text{C}_6\text{H}_4-\text{C}_6\text{H}_5$						
Entry	Base	Solvent	<i>T</i> (°C)	Yield ^a (%)	TON	TOF (h ^{−1})
1	K ₂ CO ₃	toluene	100	47		
2	KOH	toluene	100	96	960	480
3 ^b	KOH	toluene	100	93	930	465
4 ^c	KOH	toluene	100	91	910	455
5 ^d	KOH	toluene	100	94	940	470
6	K ₃ PO ₄ ·3H ₂ O	toluene	100	81		
7	K ₃ PO ₄	toluene	100	88		
8	K ₃ PO ₄ ·7H ₂ O	toluene	100	92		
9	Na ₂ CO ₃	toluene	100	0.2		
10	KOH	dioxane	100	74		
11	KOH	DMF	120	17		
12	KOH	THF	70	15		
13	KOH	H ₂ O	90	77		
14	KOH	methanol	70	90		

Reaction conditions: 4-bromotoluene (0.5 mmol), PhB(OH)₂ (0.6 mmol), base (1.0 mmol), solvent (2.0 mL), catalyst **1a** (0.1 mol%), under air for 2 h.

^a GC yields. ^b Catalyst **1b** (0.1 mol%). ^c Catalyst **2a** (0.1 mol%). ^d Catalyst **2b** (0.1 mol%).

Table 6

Suzuki coupling reactions of aryl halides with phenylboronic acid.

$\text{R}-\text{C}_6\text{H}_4-\text{X} + \text{C}_6\text{H}_5-\text{B}(\text{OH})_2 \xrightarrow[\text{Solvent, } T]{\text{Cat. } \mathbf{1a}, \text{ base}} \text{R}-\text{C}_6\text{H}_4-\text{C}_6\text{H}_5$				
Entry	ArX	Product	Yield ^a (%)	Yield ^b (%)
1	<i>o</i> -CH ₃ -C ₆ H ₄ Br		44	
2	<i>p</i> -CH ₃ -C ₆ H ₄ Br		96	94
3	<i>m</i> -NH ₂ -C ₆ H ₄ Br		41	
4	<i>p</i> -NH ₂ -C ₆ H ₄ Br		45	
5	<i>p</i> -CF ₃ -C ₆ H ₄ Br		>99	93
6	<i>p</i> -NO ₂ -C ₆ H ₄ Br		92	90
7	<i>o</i> -CN-C ₆ H ₄ Br		80	
8	<i>m</i> -CN-C ₆ H ₄ Br		56	
9	<i>p</i> -CN-C ₆ H ₄ Br		92	88
10	<i>p</i> -COCH ₃ -C ₆ H ₄ Br		95	
11	3-Br-pyridine		99	
12	3-Br-thiophene		>99	95
13	Bromo-naphthalene		58	

Reaction conditions: aryl bromide (0.5 mmol), PhB(OH)₂ (0.6 mmol), KOH (1.0 mmol), toluene (2.0 mL), catalyst **1a** (0.1 mol%), at 100 °C under air for 2 h. ^a GC yields. ^b Isolated yields.

electron-rich aryl bromides containing groups such as –CN, –CHO, –NO₂, –CF₃, and –CH₃ at the *para* position gave the coupling products in good yields (entries 2, 5, 6, 9, and 10), and those with *ortho* or *meta* substituents gave the coupling products in moderate to good yields (entries 1, 3, 7, and 8). 3-Bromofuran and 3-bromopyridine gave the coupling products in excellent yields, but 1-bromonaphthalene gave a yield of 58% (entries 11–13).

3.4. Suzuki coupling reactions in pure water

The catalytic properties of the palladacycles in Suzuki coupling reactions in water were investigated. The reaction conditions were screened using the coupling reaction of bromobenzene with phenylboronic acid, using 0.1 mol% of **1a** as a model reaction. As shown in Table 7, K₃PO₄·3H₂O, NaHCO₃, and K₃PO₄·7H₂O were found to be effective bases, giving high yields in water at 100 °C (entries 4, 7, and 9). When the reaction temperature was reduced from 100 °C to 90 and 80 °C, isolated yields of 97% and 89%, respectively, were obtained (entries 10 and 11). The relative activities of several palladacycles were investigated under the same reaction conditions using K₃PO₄·3H₂O (entries 10–13). The palladacycles all exhibited high catalytic activities for Suzuki coupling reactions under the

Table 7

Investigation of Suzuki cross-coupling reaction conditions in water.

Entry	Base	Solvent	<i>T</i> (°C)	Yield ^a (%)	TON	TOF (h ⁻¹)
1	Na ₂ CO ₃	H ₂ O	100	82		
2	K ₃ PO ₄	H ₂ O	100	70		
3	KOH	H ₂ O	100	89		
4	K ₃ PO ₄ ·3H ₂ O	H ₂ O	100	97		
5	Et ₃ N	H ₂ O	100	85		
6	K ₂ CO ₃	H ₂ O	100	45		
7	NaHCO ₃	H ₂ O	100	96		
8	NaOAc	H ₂ O	100	67		
9	K ₃ PO ₄ ·7H ₂ O	H ₂ O	100	96		
10	K ₃ PO ₄ ·3H ₂ O	H ₂ O	90	97	970	485
11 ^b	K ₃ PO ₄ ·3H ₂ O	H ₂ O	90	92	920	460
12 ^c	K ₃ PO ₄ ·3H ₂ O	H ₂ O	90	94	940	470
13 ^d	K ₃ PO ₄ ·3H ₂ O	H ₂ O	90	94	940	470
14	K ₃ PO ₄ ·3H ₂ O	H ₂ O	80	89		

Reaction condition: bromobenzene (0.5 mmol), PhB(OH)₂ (0.6 mmol), base (1.0 mmol), H₂O (2.0 mL), catalyst **1a** (0.1 mol%), under air for 2 h.^a GC yields. ^b Catalyst **1b** (0.1 mol%). ^c Catalyst **2a** (0.1 mol%). ^d Catalyst **2b** (0.1 mol%).

optimized reaction conditions.

We next examined the scope and limitations of the protocol using aryl bromides and phenylboronic acid in the presence of 0.1 mol% **1a** at 90 °C with K₃PO₄·3H₂O as the base. The obtained results are summarized in Table 8. Aryl bromides with electron-donating and electron-withdrawing *para* substituents all worked well, providing the target products in good to excellent yields after 2 h (entries 2, 4, 6, 8, 12, and 13). The coupling reactions also proceeded smoothly with 3-bromopyridine, 3-bromothiophene, and 1-bromonaphthalene under the same reaction conditions to afford the coupling products in modest

Table 8

Suzuki coupling reactions of aryl bromides with phenylboronic acid in water.

Entry	ArX	Product	Yield ^a (%)	Yield ^b (%)	Entry	ArX	Product	Yield ^a (%)	Yield ^b (%)
1	<i>o</i> -CH ₃ -C ₆ H ₄ Br		67		9	<i>o</i> -CN-C ₆ H ₄ Br		96	
2	<i>p</i> -CH ₃ -C ₆ H ₄ Br		97	94	10	<i>m</i> -CN-C ₆ H ₄ Br		76	
3	<i>m</i> -NH ₂ -C ₆ H ₄ Br		60		11	<i>p</i> -CN-C ₆ H ₄ Br		86	85
4	<i>p</i> -NH ₂ -C ₆ H ₄ Br		91		12	<i>p</i> -CF ₃ -C ₆ H ₄ Br		99	95
5	<i>o</i> -OCH ₃ -C ₆ H ₄ Br		47		13	<i>p</i> -NO ₂ -C ₆ H ₄ Br		92	
6	<i>p</i> -OCH ₃ -C ₆ H ₄ Br		71	68	14	3-Br-pyridine		71	
7	<i>o</i> -CHO-C ₆ H ₄ Br		75		15	3-Br-thiophene		85	
8	<i>p</i> -CHO-C ₆ H ₄ Br		87	82	16	Bromo-naphthalene		65	

Reaction conditions: aryl bromide (0.5 mmol), PhB(OH)₂ (0.6 mmol), K₃PO₄·3H₂O (1.0 mmol), H₂O (2.0 mL), catalyst **1a** (0.1 mol%), at 90 °C under air for 2 h. ^a GC yields. ^b Isolated yields.**Table 9**

Suzuki coupling reactions of aryl chlorides and iodides with phenylboronic acid in water.

X = Cl, I			
Entry	ArX	Product	Yield ^a (%)
1	C ₆ H ₅ Cl		24
2	<i>p</i> -CH ₃ O-C ₆ H ₄ Cl		45
3	<i>p</i> -CH ₃ CO-C ₆ H ₄ Cl		35
4	<i>m</i> -CH ₃ O-C ₆ H ₄ Cl		6
5	<i>p</i> -HOOC-C ₆ H ₄ I		trace
6	C ₆ H ₅ I		79

Reaction conditions: aryl chlorides or iodides (0.5 mmol), PhB(OH)₂ (0.6 mmol), K₃PO₄·3H₂O (1.0 mmol), H₂O (2.0 mL), catalyst **1a** (0.1 mol%), at 90 °C under air for 2 h. ^a Isolated yields.

to good yields (entries 14–16). However, sterically hindered aryl bromides containing *ortho* or *meta* substituents gave the coupled product in slightly lower yields (entries 1, 3, 5, and 7). Interestingly, 2-bromobenzonitrile, 3-bromobenzonitrile, and 4-bromobenzonitrile provided the coupled product in 96%, 76%, and 66% yields, respectively (entries 9–11).

Finally, the reactions of aryl chlorides or iodides with phenylboronic acid in water were also tested. The results are summarized in Table 9. Aryl chlorides gave the corresponding coupling products in low yields (entries 1–4). Iodobenzene reacted with phenylboronic acid to give the coupling product in

79% yield, and 4-iodobenzoic acid was found to be a poor coupling partner (entries 5 and 6). This is probably because 4-iodobenzoic acid was highly reactive and failed to undergo cross-coupling in our catalytic system.

4. Conclusions

A series of cyclopalladated ferrocenylimines dimers and monomers with ester groups were designed and prepared. We also developed a convenient and efficient methodology for Suzuki and Heck coupling reactions of aryl bromides catalyzed by cyclopalladated ferrocenylimines with ester groups in organic solvents or water under ambient conditions with low catalyst loadings of 0.1 mol%. Suzuki coupling reactions in water at 90 °C in the absence of additives are significant in terms of both economics and the environment.

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Graphical Abstract

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Cyclopalladated ferrocenylimines with ester group for Heck and Suzuki coupling reactions

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Cyclopalladated ferrocenylimines with ester groups were prepared and effectively catalyzed Heck and Suzuki coupling reactions of aryl or heteroaryl halides in water or organic solvents.

含有酯基二茂铁亚胺环钯化合物催化Suzuki和Heck反应

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摘要: 合成并表征了系列含有酯基二茂铁亚胺环钯化合物. 结果表明, 该系列环钯催化剂在纯水或有机溶剂中均能高效催化Heck和Suzuki偶联反应.

关键词: Suzuki偶联反应; Heck偶联反应; 环钯二茂铁亚胺

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